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DRINKER BIDDLE & REATH
ONE LOGAN SQUARE
18TH AND CHERRY STREETS
PHILADELPHIA, PA 19103-6996

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| EXAMINER |
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NICKOL, GARY B

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| ART UNIT | PAPER NUMBER |
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1642

DATE MAILED: 02/26/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/670,128

Applicant(s)

REDDY ET AL.

Examiner

Gary B. Nickol Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 January 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-39 is/are pending in the application.
- 4a) Of the above claim(s) 1-12, 14 and 17-39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 13, 15 and 16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

The Election filed January 11, 2002 (Paper No. 9) in response to the Office Action of December 11, 2001 is acknowledged and has been entered. Claims 1-29 are pending in the application and Claims 1-12, 14, 17-29 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions. Claims 13, 15-16 are currently under prosecution

Applicant's election with traverse of Group IV, claims 11-13, 15-16 in Paper No 9 is acknowledged with a species election of determining a metastatic potential. The traversal is on the ground(s) that the inventions have not been shown to be independent and the examination of Groups I through IV or Groups V-VIII would not impose a serious burden on the examiner. This is not found persuasive. MPEP 802.01 provides that restriction is proper between inventions which are independent or distinct. Here, the inventions of the various groups are distinct for the reasons set forth in Paper No. 9.

As to the question of burden of search, the inventions are classified differently, necessitating different searches in the literature. And although some Groups have similar classification, the classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not coextensive and is much more important in evaluating the burden of search. Different searches and issues are involved in the examination of each group. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Specification

The specification is objected to for the following reason: The specification on page 1 should be amended to reflect the priority status of the present application, for example:

This application is a continuation of PCT/US99/06514, filed March 25, 1999 which claims the benefit of U.S. provisional application 60/079,755 filed March 27, 1998, now abandoned.

Claim Objections

Claim 13 is objected to because of the following informalities: Claim 13 recites "afflicted patient afflicted". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13, 15-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13, 15-16 are rejected as vague and indefinite for reciting "metastatic potential" as the specification does not clearly define nor limit the metes and bounds of what encompasses determining a metastatic potential. Although the specification teaches (page 11, line 6) that tumors which exhibit a hormone-dependent pattern are less malignant, less metastatic, and

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generally more readily treatable than hormone-independent tumors, such teaching do not limit that which encompasses determining a metastatic potential. All malignant cancers are potentially metastatic and is not clear from the specification how the steps of the method clearly determine what cancers may or may not comprise a metastatic potential. Thus, the metes and bounds of the claim cannot be determined.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 13, 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garcia *et al.* (Cell Growth & Differentiation, Vol.8, pages 1267-1276, December 1997, IDS) and Takemoto *et al.* (Proc.Natl.Acad.Sci., Vol. 94, December 1997, pages 13897-13902).

The claims are drawn to a method for determining the metastatic potential of a cancer in an afflicted patient comprising determining the level of activated STAT-3 protein in a sample from the patient, an increased level of said protein being indicative of the metastatic potential of said tumor (Claim 13); wherein determining the level of activated STAT-3 protein comprises determining the relative level of phosphorylated STAT 3 protein (Claim 14); wherein the level of phosphorylated STAT-3 protein is determined by contacting the sample with an antibody which binds said phosphorylated protein (Claim 15).

1. Garcia *et al.* teach that elevated STAT3 activity was present in five of nine breast carcinoma cell lines examined but not in any of three cell lines derived from normal breast epithelial tissue (page 1271, 1st column). Garcia's methods employed determining the relative level of phosphorylated STAT 3 protein by contacting the samples with an antibody which binds the phosphorylated protein (see Figure 8, Lane C). Garcia *et al.* further teach that studies of "primary tumors" indicate that elevated STAT3 activation also occurs in human breast tumors compared to adjacent normal tissue (page 1274, 1st column, 1st paragraph) and that, overall, constitutive activation of Stat3 is a frequent event in breast carcinoma cells.
2. Garcia *et al.* do not teach patient sampling of STAT3 as an indicator of the metastatic potential.
3. Takemoto *et al.* sample activated STAT3 proteins from cancer patients (Figure 2, page 13900) and further report that that the "cells of three patients, whose extracts revealed constitutive activation of STAT proteins, actively synthesized DNA, whereas in the case of patient 2, the absence of STAT activation was consistent with a much lower

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percentage of cells in S phase and 94% of cells arrested in G₀/G₁.” (page 13900, last sentence).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modulate the method of Garcia *et al.* so as to sample STAT3 protein from a patient “afflicted” with breast cancer in order to determine the metastatic potential of the cancer. One would have been motivated to do so because Garcia *et al.* teach that studies of “primary tumors” indicate that elevated STAT3 activation also occurs in human breast tumors compared to adjacent normal tissue and that, overall, constitutive activation of Stat3 is a frequent event in breast carcinoma cells. Moreover, from direct assays of cancer patients, Takemoto *et al.* clearly teach that constitutive activation of Stat3 is also consistent with increased DNA synthesis, an indicator of the metastatic and aggressive potential of tumor cells. Taken together, the combination of the two references suggest to one of ordinary skill in the art a reasonable expectation of success by determining the level of activated Stat3 in patients afflicted with cancer in order to determine the metastatic potential of the cancer since increased DNA synthesis is consistent with activated Stat3.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143.

The examiner can normally be reached on M-F, 8:30-5:00 P.M..


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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
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GBN
February 20, 2002


ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600